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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,697	08/05/2003	Pablo Umana	1975.0010005/TJS/AWL	5455

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EXAMINER	
GUZO, DAVID	
ART UNIT	**PAPER NUMBER**
1636	
MAIL DATE	**DELIVERY MODE**
10/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/633,697	UMANA ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/12/08,7/2/08,9/10/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *167-234* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *167-234* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/12/08,7/2/08,9/10/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 167-173, 175, 177, 179, 197-202, 218-229 and 231-234 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rothman et al. in view of Goldenberg (US 6,183,744).

Applicants claim a method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing *N*-linked oligosaccharides;

(b) glycoengineering said host cell so that said host cell has a decreased level of activity of at least one glycoprotein-modifying glycosyltransferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Rothman et al. (Mol. Immunol., 1989, Vol. 26, No. 12, pp. 1113-1123, see whole article, particularly the Abstract, pp. 1114, 1119-1122) teaches a method for producing a full length antibody (i.e. having heavy and light chains, Fc region having *N*-linked oligosaccharides, CH2 domain, directed against human melanoma antigens, etc.) having increased Fc mediated cellular cytotoxicity (more than 80% increase) or increased Fc receptor binding affinity, said method comprising providing a host cell that expresses an antibody comprising an IgG Fc region containing N-linked oligosaccharides, glycoengineering the cell by culturing the cell in the presence of glycosylation and carbohydrate processing inhibitors (castanospermine, N-methyldeoxynojirimycin, deoxymannojirimycin, monesin), culturing the cell so as to produce the antibody and isolating the antibody. Rothman et al. does not teach expression of **recombinant** antibodies with increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity. It is noted that the inhibitors used by Rothman et al. interfere with early steps in carbohydrate processing or in the maturation of protein

bound oligosaccharides, etc. Therefore, the cells have a decreased level of activity of glycoprotein-modifying glycosyltransferases. Also, given the interference with **early steps in carbohydrate processing** and absent evidence to the contrary, the activity of glycoprotein-modifying glycosyltransferases such as α-mannosidase II, β(1,4)-N-acetylglucosaminyltransferase III, β(1,4)-galactosyltransferase, etc. in cells treated with said inhibitors must be assumed to be decreased.

Goldenberg (priority to 3/24/1997, see whole document, particularly columns 3-6, Claims 1-23, etc.) teaches the well known methods of making (using recombinant DNA expression vectors) and using recombinant monoclonal antibodies (such as anti-CD20 or CD22, etc.), antibody fragments, fusions of antibody sequences with other proteins, humanized antibodies, chimeric antibodies, therapeutic antibodies, etc. and use of said recombinant antibodies for immunotherapy of B-cell malignancies. It is noted that the Goldenberg reference is only one example from among hundreds of references detailing the generation of recombinant antibodies.

The ordinary skilled artisan, seeking to generate improved recombinant therapeutic antibodies for treatment of cancers or other malignancies, such as those disclosed by Goldenberg, would have been motivated to generate said recombinant antibodies in cells glycoengineered by the method of Rothman et al. so as to enhance the Fc mediated antibody-dependent cytotoxicity mediated by natural killer cells. It would have been obvious for the ordinary skilled artisan to do this because increasing the Fc mediated antibody-dependent cytotoxicity of recombinant therapeutic antibodies by glycoengineering the cells which produce said antibodies, wherein said

glycoengineering comprises culturing said antibody producing cells in the presence of glycosylation and carbohydrate processing inhibitors, would increase the therapeutic efficacy of said antibodies against cancer cell targets.

Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 216 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rothman et al. in view of Goldenberg and Brams et al.

Applicants' invention is as described above. In addition, applicants recite that the host cell is an engineered CHO cell.

Rothman et al. and Goldenberg are applied as above. Neither reference teaches using a CHO cell to produce the recombinant antibody having increased Fc mediated cellular cytotoxicity.

Brams et al. (US 5,939,068, issued 8/17/1999, filed 4/18/1996, see whole document, particularly columns 9-11) teaches preferential use of CHO cells engineered to express recombinant antibodies.

The ordinary skilled artisan, seeking to choose a host cell for expression of the recombinant antibodies described by Rothman et al. and Goldenberg, would have been motivated to choose CHO cells because Brams et al. teaches that engineered CHO cells are preferred cells for expression of recombinant antibodies. It would have been

obvious for the ordinary skilled artisan to do this because Brams et al. teaches that CHO cells are preferred cells for expression of recombinant antibodies. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Obviousness Type Double Patenting Rejections

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 170-234 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 228-260 of copending Application No. 10/761,435. Although the conflicting claims are not identical,

they are not patentably distinct from each other because of reasons of record in the previous Office Action.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants do not traverse the rejection but argue that if the instant provisional obviousness type double patenting rejection is the only remaining rejection in the earlier filed of the two applications, said rejection should be withdrawn and the case passed to issue.

Applicants arguments filed 5/12/08 have been considered but are not persuasive. Since the instant provisional obviousness type double patenting rejection is not the only remaining rejection, said rejection stands.

Claims 167-234 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 159-167 of copending Application No. 10/633,699. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims recite methods of producing recombinant antibodies having increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding compared to a corresponding antibody that has not been glycoengineered wherein said methods comprise genetically manipulating said host cell to alter the activity of a glycoprotein-modifying glycosyltransferase. The limitations of the instant claims with regard to the glycoprotein-modifying glycosyltransferases manipulated so as to generate the recombinant antibodies, the

host cells, the types of altered glycoproteins on the antibodies, etc. are all species disclosed in the '699 application and could have been claimed in said application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any rejections not repeated in this Office Action are withdrawn.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D., can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 19, 2008

/David Guzo/
Primary Examiner
Art Unit 1636